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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants : David M. Stern, et al.,  
U.S. Serial No.: 09/638,648 Examiner: T.N. Ton  
Filed : August 14, 2000  
For : A METHOD TO INCREASE CEREBRAL BLOOD FLOW IN  
AMYLOID ANGIOPATHY

1185 Avenue of the Americas  
New York, New York 10036  
June 15, 2001

Assistant Commissioner for Patents  
Washington, D.C. 20231

Sir:

INFORMATION DISCLOSURE STATEMENT

In accordance with the duty of disclosure under 37 C.F.R. §1.56, applicants would like to direct the Examiner's attention to the following documents, which are listed hereinbelow and again listed on Form PTO-1449 attached hereto as **Exhibit A**. Copies of the documents listed below are attached hereto as **Exhibits 1-20**.

1. Morser et al., U.S. Patent No. 5,864,018, filing date April 16, 1996.
2. Morser et al. PCT International Application No. PCT/EP97/01834, filed April 11, 1997, published October 23, 1997; Publication No. WO 97/39125, Antibodies Against the Advanced Glycation Endproduct Receptor and Uses Thereof.

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3. Morser et al. PCT International Application No. PCT/EP97/01832, filed 11 April 1997, published October 23, 1997, Publication No. WO 97/39121, Advanced Glycation Endproduct Receptor Peptides and Uses Thereof.
4. Stern et al., PCT International Publication No. WO 97/26913, published July 31, 1997, PCT International Application No. PCT/US97/00857 (Attny Dkt 48316-PCT).
5. Stern, D., AM Schmidt and Jun Wu - A Method For Treating Symptoms Of Diabetes In A Subject (PCT/US97/21197, filed November 12, 1997) (Attny Dkt. 50159-PCT).
6. Stern, D., Shi Du Yan, Ann Marie Schmidt - PCT International Application No. PCT/US98/21346; filed 09 OCT 98; Ligand Binding Site of RAGE, (Attny Dkt. 53447-PCT).
7. Stern, D., Yan, S-D. and Schmidt, A. M., U.S. Serial No. 09/374,213, filed August 13, 1999, A Method of Preventing Amyloid Disturbance of Cellular Properties and for Clearing Amyloid from Tissue (Attny. Dkt. 59472).
8. Gheresi-Egea JF, Gorevic PD, Ghiso J, Frangione BF, Patlak CS, Fenstermacher JD. Fate of cerebrospinal fluid-borne amyloid  $\beta$ -peptide: rapid clearance into blood and appreciable accumulation by cerebral arteries J Neurochem 1996;67:880-83.

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10. Holtzman DM, Bales KR, Wu S, Bhat P, Parsadanian M, Fagan AM, Chang LK, Sun Y, Paul SM. In Vivo expression of apolipoprotein E reduces amyloid- $\beta$ -deposition in a mouse model of Alzheimer's Disease. *J Clin Invest* 1999; 103:R15-21.
11. Mackic JB, Weiss MH, Miao W, Ghiso J, Calero M, Bading J, Frangione B, Zlokovic BV. Cerebrovascular accumulation and increased blood-brain barrier permeability to circulating Alzheimer's amyloid- $\beta$  peptide in aged squirrel monkey with cerebral amyloid angiopathy. *J Neurochem* 1998;70:210-5.
12. Mackic JB, Stins M, McComb JG, Calero M, Ghiso J, Kim KS, Yan SD, Stern D, Schmidt AM, Frangione B, Zlokovic BV. Human blood-brain barrier receptors for Alzheimer's amyloid- $\beta$ <sub>1-40</sub>: asymmetrical binding, endocytosis and transcytosis at the apical side of brain microvascular endothelial cell monolayer. *J Clin Invest* 1998;102:734-743.
13. Neeper, M., et al. (1992). Cloning and expression of a cell

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14. Poduslo JF, Curran GL, Haggard JJ, Biere AL, Selkoe DJ. Permeability and residual plasma volume of human, Dutch variant, and rat amyloid  $\beta$ -protein 1-40 at the blood-brain barrier. *Neurobiol Dis* 1997;4(1):27-34.
15. Schmidt, A-M, et al. (1992) "Isolation and characterization of binding proteins for advanced glycation endproducts from lung tissue which are present on the endothelial cell surface" *J. Biol. Chem.*, 267:14987-14997.
16. Schmidt AM, Hasu M, Popov D, Zhang JH, Chen J, Yan SD, Brett J, Cao R, Kuwabara K, Gostache G, Simionescu N, Simionescu M, Stern D. Receptor for advanced glycation end products (AGE) has a central role in vessel wall interactions and gene activation in response to circulating AGE proteins. *Proc Natl Acad Sci USA* 1994;91:8807-11.
17. Yan SD, Chen X, Fu J, Chen M, Zhu H, Roher A, Slattery T, Zhao L, Nagashima M, Morser J, Migheli A, Nawroth P, Stern D, Schmidt AM. RAGE and amyloid- $\beta$  peptide neurotoxicity in Alzheimer's disease. *Nature* 1996;382:685-91.
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20. Zlokovic BV. Cerebrovascular permeability to peptides:  
manipulations of transport systems at the blood-brain barrier.  
Pharm Res 1995; 12(10): 1395-1406.

Applicants request the Examiner make these references of record.

If a telephone interview would be of assistance in advancing  
prosecution of the subject application, applicants' undersigned  
attorneys invite the Examiner to telephone at the number provided  
below.

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No fee is deemed necessary in connection with the filing of this Information Disclosure Statement. If any additional fees are required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,

*Jane M. Love*

I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to:  
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